In the Drawings

Applicants respectfully propose an amendment to Figure 8A as shown in revised formal drawing page marked "Replacement Sheet". Entry of the proposed amendment to the drawing is respectfully requested.

REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office action dated October 9, 2003 are respectfully requested.

I. Amendments

Claim 18 is amended to recite a native monocot Gt1 seed-specific promoter as recited on page 20, lines 26-27.

Figure 8A is amended to recite that the UAS is a 98 bp fragment from the Glb promoter. Support for this amendment can be found on page 31, lines 15-19.

II. Rejection under 35 U.S.C. §112, first paragraph

Claims 18 and 23-24 were rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 18 and 23-24 were further rejected under 35 U.S.C. §112, first paragraph, allegedly because the specification does not enable any person skilled in the art to which it pertains, or with which it is most connected to make and use the invention commensurate in scope with the claims.

These rejections are respectfully traversed.

A. Written Description

The Examiner asserts that the specification fails to provide an adequate written description of the invention as claimed. The claims, as amended, are directed to a method of making a modified Gt1 seed-specific promoter responsive to a Reb transcription factor.

1. Legal Standard for Written Description

According to MPEP 2163.02, an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Unlike the "enablement" requirement, the "written description" requirement of 35 U.S.C. §112, first paragraph is not concerned with support commensurate with the breadth of the claims. The essential purpose of the written description requirement is to show the possession of the invention as of the filing date as a *prima facie* date of invention. *In re Smith*, 481 F.2d 910, 178 U.S.P.Q. 620,623 (CCPA 1973). Accordingly, the specification is required to contain a statement that adequately describes the invention as claimed. However, the invention need not be described in *ipsis verbis* in order to satisfy the description requirement. See *In re Lukach, Olson, and Spurlin*, 169 U.S.P.Q. 795, 796 (CCPA 1971).

2. Meeting the Legal Standard

The claimed method of making a modified Gt1 seed-specific promoter responsive to a Reb transcription factor includes the steps of (i) determining the native response sequence for the Reb transcription factor, (ii) providing a heterologous nucleic acid construct comprising a native monocot Gt1 seed-specific promoter that does not respond to the Reb transcription factor, and (iii) inserting the response sequence into the Gt1 promoter resulting a modified Gt1 promoter which is effective to bind the Reb transcription factor.

Step (i) requires that the native response sequence for the Reb transcription factor be determined. On page 18, line 25 and Example 1, the inventors describe isolating a Reb gene from a bacterial artificial chromosome (BAC) library. Or, as described on page 18, lines 19-24, the Reb gene can be obtained from the literature, as

it was cloned by Nakase *et al.* (Plant Mol. Biol., 33(3):513-522 1997) and is publicly available as Accession No. AB021736 at the Genbank database (www.ncbi.nlm.nih.gov/Genbank/index.html). Determination of the response sequence for Reb (UAS) by band shift assay is described in the specification (see page 19, lines 10-13). Also, determination of Reb binding sites for determining the response sequence is described in detail in Nakase *et al.* Function of an UAS is confirmed through loss-of-function and gain-of-function experiments (see page 19, lines 11-13 and Example 2). Using these methods, one can readily determine the response sequence for any Reb transcription factor. Accordingly, based on the guidance in the specification at the time of filing, one of skill in the art would reasonably conclude that Applicants were in possession of "determining the native response sequence for the Reb transcription factor."

With respect to step (ii), "providing a heterologous nucleic acid construct comprising a native monocot Gt1 seed-specific promoter that does not respond to the Reb transcription factor", Applicants note that preparation of a heterologous nucleic acid construct is well within the knowledge and skill of one skilled in the art as exemplified by the standard manual Sambrook and Maniatis, Molecular Cloning, Cold Spring Harbor Laboratory, Cold Spring Harbor, 1989 and Ausubel *et al.* Current Protocols in Molecular Biology, John Wiley & Sons, New York, N.Y., (c) 1987, 1988, 1989, 1990, 1993. Further, heterologous nucleic acid constructs are generally described on page 19, lines 22-33 of the specification. Additional components are described on pages 19-20. Sequences for native monocot Gt1 seed-specific promoters are obtainable in the literature or in public databases as evidenced by Accession No. AY387493 for *Zea mays* (corn) available at the Genbank database. On page 22, lines 11-14, it is described that a promoter such as the Gt1 promoter may be isolated from other extracts, e.g. wheat, oat, or the like using conventional hybridization techniques known in the art. Exemplary methods of determining whether the Gt1 seed specific promoter responds to the Reb transcription factor are listed as scanning the Gt1 promoter sequence for a Reb binding motif (page 31, lines 13-14) and preparing a Gt1 promoter linked to a gene and testing by co-bombardment of developing endosperm with the Reb

gene to measure for expression of the gene linked to the Gt1 promoter. Accordingly, one of skill in the art would reasonably conclude that Applicants were in possession of "providing a heterologous nucleic acid construct comprising a native monocot Gt1 seed-specific promoter that does not respond to the Reb transcription factor" at the time of filing the application.

Step (iii) of the claims requires that the Reb response sequence is inserted into the native monocot Gt1 seed-specific promoter, resulting in a modified Gt1 seed-specific promoter which is effective to bind the Reb transcription factor. A specific embodiment is described where a 98 bp Reb response sequence is inserted at a position –630 bp distal to the TATA box of the Gt1 promoter. Investigation of promoters including active sites and binding regions is within the knowledge of one skilled in the art and detailed in the literature. For example the linker scanning method is an *in vitro* method that is known in the literature (e.g. Sharp and Garcia, *Mol Cell Biol.*, 8(3):1266-1274, 1988) that can be used to determine an insertion site for the Reb response sequence without affecting the activity of the promoter. Accordingly, one of skill in the art would reasonably conclude that at the time of filing Applicants were in possession of "inserting the response sequence into the Gt1 promoter resulting a modified Gt1 promoter which is effective to bind the Reb transcription factor."

The Examiner further asserts that Applicants have not disclosed the 98 bp sequence or how one isolates the sequence from a Glb promoter. Applicants respectfully direct the Examiner to page 31, lines 17-18, where the 98 bp sequence is described as spanning the three copies of the identified Reb binding motifs. As noted above, isolation of the binding motifs is described in Nakase et al. and specifically described on page 31, line 18. Methods for determination of a response sequence for Reb (UAS) by band shift assay is described on page 19, lines 10-13.

In view of the teachings in the specification, one skilled in the art would reasonably conclude that Applicants were in possession of the claimed invention at the time the invention was filed. Withdrawal of the rejection of the claims under 35 U.S.C. §112, first

paragraph as allegedly containing subject matter which was not described in the specification at the time of filing is respectfully requested.

B. Enablement

1. Legal Standard for Enablement

The first paragraph of 35 U.S.C. §112 requires that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention without undue experimentation (e.g., *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir., 1991).

The enablement requirement is met if the description enables any mode of making and using the claimed invention (*Engel Industries, Inc. v. Lockformer Co.,* 946 F.2d 1528, 20 USPQ2d 1300 (Fed. Cir. 1991).

An invention is enabled even though the disclosure may require some routine experimentation to practice the invention. *Hybritech Inc,* V. *Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). The fact that the required experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *MLT. v A.B. Fortia,* 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985).

2. Meeting the Legal standard

In accordance with the accepted standards of enablement set out above, an invention is enabled if one skilled in the art could make and use the claimed invention without undue experimentation.

a. How to make requirement:

In practicing the methods of the invention, as embodied in amended claim 18, one skilled in the art would have to make or provide for a modified Gt1 seed-specific promoter responsive to a Reb transcription factor by carrying out the steps of:

(i) determining the native response sequence for the Reb transcription factor;

(ii) providing a heterologous nucleic acid construct comprising a native monocot Gt1 seed-specific promoter which does not respond to said Reb transcription factor; and

(iii) inserting the response sequence into said native Gt1 seed-specific promoter, resulting in the modified Gt1 seed-specific promoter, which is effective to bind said Reb transcription factor, wherein the binding of the Reb transcription factor to said response sequence results in an increase in the expression of a gene under the control of said Gt1 seed-specific promoter.

The specification provides ample guidance for one of skill to make each of these elements.

With regard to (i), the inventors provide guidance, first, on how to isolate a Reb gene (page 18, line 25 and Example 1). Further, the sequence of Reb gene is publicly available in the literature and on public databases (Nakase *et al.* and Accession No. AB021736. Guidance for determination of the response sequence for Reb (UAS) by band shift assay is then described on page 19, lines 10-13. Second, guidance for methods for determination of Reb binding sites for determining the response sequence are described in Nakase *et al.* Guidance for exemplary methods for confirmation of function of an UAS through loss-of-function and gain-of-function experiments is given on page 19, lines 11-13 and Example 2 of the specification.

These methods could be used to routinely and predictably determine the response sequence for any Reb transcription factor. Accordingly, one of skill in the art has ample guidance for "determining the native response sequence for the Reb transcription factor."

With regard to (ii), methods for preparation of a heterologous nucleic acid construct are well-known to one skilled in the art. Further, the specification gives ample guidance for making heterologous nucleic acid constructs on page 19, lines 22-33. Guidance for additional components is given on pages 19-20. Applicants have provided the native Gt1 sequence for *Oryza sativa* (SEQ ID NO: 26). Sequences for native monocot Gt1 seed-specific promoters are additionally obtainable in the literature or in public databases as evidenced by Accession No. AY387493 for *Zea mays* (corn) available at the Genbank database. Guidance for determining whether the Gt1 seed-specific promoter responds to the Reb transcription factor is described on page 31, lines 13-14. Guidance for testing the modified Gt1 promoter by co-bombardment of

developing endosperm with the Reb gene to measure for expression of the gene linked to the Gt1 promoter is a routine procedure.

As described, the specification provides ample guidance for finding Gt1 seed specific promoters, determining whether the Gt1 seed-specific promoter responds to a Reb transcription factor, and for making heterologous nucleic acid constructs. Accordingly, one of skill in the art has ample guidance for "providing a heterologous nucleic acid construct comprising a native monocot Gt1 seed-specific promoter that does not respond to the Reb transcription factor."

In step (iii) of the claims, the Reb response sequence is inserted into the native monocot Gt1 seed-specific promoter, resulting in a modified Gt1 seed-specific promoter which is effective to bind the Reb transcription factor. The Examiner will appreciate that it is well within the knowledge of one of skill in the art to use routine techniques and methods for investigation of promoters including active sites and binding regions. These methods are further detailed in the literature. For example the linker scanning method is a routine and predictable *in vitro* method that is known in the literature (e.g. Sharp and Garcia, *Mol Cell Biol.*, 8(3):1266-1274, 1988) that can be used to determine an insertion site for the Reb response sequence without affecting the activity of the promoter. Kits for linker scanning are even publicly available as evidenced by the EZ::TN In-Frame Linker Insertion Kit from EPICENTRE (Madison, WI). Guidance for determining if a modified Gt1 promoter is effective to bind the Reb transcription factor is given on page 31, lines 20-25.

Accordingly, the specification gives ample guidance to one of skill in the art for "inserting the response sequence into the Gt1 promoter resulting a modified Gt1 promoter which is effective to bind the Reb transcription factor."

The Examiner acknowledges that the specification is enabling for a modified Gt1 promoter comprising the UAS fragment described on page 30, line 34 through page 31, line 36. However, the Examiner argues that the specification does not provide enablement for a method of making any modified Gt1 seed-specific promoter

responsive to any Reb transcription factor from any plant. As shown above, the specification gives ample guidance for the scope of the claims to one of skill in the art.

The Examiner further asserts that Applicants have not taught any other UAS elements that any Reb transcription factor will bind. Applicants have, however, given ample guidance for determining other binding elements for Reb, for example, using band-shift assay.

In response to the Examiner's assertion that "Promoters are very sensitive to random insertions, single base insertions can ablate promoter function", Applicants submit that routine and predictable methods for investigating promoter function and determining insertion areas are well known to one of skill in the art.

With regard to the discrepancy between Fig. 8A and page 31, lines 15-19, Applicants have amended Fig. 8A to recite a 98 bp fragment in accord with the Examiner's kind suggestion.

Applicants submit that the specification teaches one of skill in the art how to make a transgenic fruit-bearing plant that exhibits enhanced expression of a gene the expression of which is associated with a morphological characteristic without undue experimentation.

b. How to use requirement:

With respect to the use of the modified Gt1 promoter, Example 2 provides an actual reduction to practice of the invention. Further guidance for use of the invention is given on page 14, lines 3-12, where it is described that a native promoter may be modified such that the modified promoter is activated by a particular transcription factor.

Accordingly, Applicants submit that the specification would enable any person skilled in the art to which it pertains to make and use the claimed invention.

In light of the teaching in the specification and Applicant's amendments, Applicants submit that the present claims satisfy the requirements of §112, first paragraph and respectfully request that the rejections be withdrawn.

III. Conclusion

In view of the foregoing, Applicants submit that the claims pending in the application are in condition for allowance. A Notice of Allowance is therefore respectfully requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted,

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Date: Dec. 12, 2003

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